CASWELL FILE

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

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OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Avermectin (Also Called Abamectin) - 89-FL-08 - Section 18 Request to Use Avermectin on Celery in Florida

Caswell No.: 63AB
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12/1/88

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The State of Florida requests a FIFRA section 18 specific exemption for the use of avermectin to control two-spotted spider mites on approximately 20 percent of the celery acreage statewide from now to July 31, 1989.

The formulation to be used is Agrimec 0.15 EC. Inerts are cleared under §180.1001.

Agrimec 0.15 EC will be applied by ground equipment at an application rate of 0.01-0.02 lbs. a.i./A. A total of up to 10 applications will be made on 1200 acres. This will result in up to 225 lbs of active ingredient being used. The proposed action level is 0.035 ppm on celery.

1

No permanent tolerances have been established for avermectin. Temporary tolerances and EUP programs are currently in effect for citrus and cotton.

The label for section 18 for celery is correct with respect to signal word, precautionary labeling, and Statement of Practical Treatment. A copy of the label is attached.

In the Dykstra memorandum of April 23, 1987, the margins of safety (MOSs) for mixer/loader and sprayers (both with and without gloves) range from 350 to 1163 when maternolethality is the toxic endpoint and from 1399 to 4651 when cleft-palate (a developmental effect) is the toxic endpoint. Based on oral communication on November 28, 1988 with C. Lunchick of the Non-Dietary Exposure Branch regarding expected exposure to workers in the section 18 use for celery, it was concluded that the exposure to workers including pickers, in the section 18 use for celery would be less than the exposure to workers in the citrus EUP program. Therefore, the MOSs for workers in the section 18 use for celery are acceptable (greater than 100).

Pivotal toxicity data which were available in support of the temporary tolerances and EUP programs are listed below:

- Rat Acute Oral $LD_{50}$: 10.6 mg/kg (males); 11.3 mg/kg (females);
- Dermal Sensitization in Guinea Pig (Abamectin): negative for skin sensitization;
- 14-Week Oral Rat Study: NOEL $\geq$ 0.4 mg/kg/day (HDT);
- 18-Week Oral Dog Study: NOEL = 0.25 mg/kg/day;
- 1-Year Dog Study: NOEL = 0.25 mg/kg/day;
- Rat Teratology Study (Abamectin): negative for terata up to 1.6 mg/kg/day (HDT);
- Rabbit Teratology Study (Abamectin): negative for terata up to 2.0 mg/kg/day (HDT);
- Mouse Teratology Study (Abamectin): teratogenic LEL = 0.4 mg/kg/day (cleft-palate); teratogenic NOEL = 0.2 mg/kg/day;

- Mouse Teratology Study (delta-8,9-isomer): teratogenic LEL = 0.10 mg/kg/day (cleft-palate); teratogenic NOEL = 0.06 mg/kg/day;

- Mouse Maternotoxicity Study (Abamectin): LEL = 0.075 mg/kg/day (lethality); NOEL = 0.05 mg/kg/day;

- Mouse Maternotoxicity Study (delta-8,9-isomer): LEL = 0.50 mg/kg/day (lethality); NOEL = 0.10 mg/kg/day;

- Two-Generation Rat Reproduction Study: NOEL = 0.12 mg/kg/day;

- Rat Metabolism Study;

- Ames Mutagenicity Assay (Abamectin): negative;

- Mutagenicity Assay for Chromosomal Aberration In Vitro in Chinese Hamster Ovary Cells: negative;

- Mammalian Cell Mutagenic Assay (Abamectin): negative for V-79 cells;

- Rat Hepatocyte Mutagenicity Study (Abamectin): under conditions of the study, abamectin (0.3 and 0.6 mM) caused an induction of single strand DNA breaks in rat hepatocytes in vitro; no effect was observed when the assay was carried out on hepatocytes from rats dosed in vivo at the $LD_{50}$ dose level (10.6 mg/kg); and

- In Vivo Bone Marrow Mutagenicity Cytogenetic Study: negative in male mice at doses of 1.2 and 12.0 mg/kg.

Additionally, preliminary evaluation of a 94-week chronic toxicity/oncogenicity mouse study and a 2-year chronic toxicity/oncogenicity rat study did not reveal any potential oncogenic effects.

Toxicological studies with the delta-8,9-isomer and polar degradates of avermectin are required before permanent tolerances can be established.

The provisional acceptable daily intake (PADI) is based on the NOEL of 0.12 mg/kg/day in the two-generation rat reproduction study. A thousandfold safety factor was used to calculate the PADI. At the LEL of 0.40 mg/kg/day in the study, effects included increase retinal folds in the weanlings, increase of dead pups, decreased viability indices, decreased lactation indices, and decreased pup body weight.

$$PADI = \frac{NOEL}{SF}$$

$$PADI = \frac{0.12 \text{ mg/kg/day}}{1000}$$

$$PADI = 0.00012 \text{ mg/kg/day}$$

A new TAS analysis and menu screen analysis are required from the Special Analysis and Outreach Section of the Science Analysis and Coordination Branch. These analyses are needed to determine the percent PADI utilized and MOS for developmental toxicity and maternolethality.

Conclusion and Recommendation

If the Science Analysis and Coordination Branch can conclude that the percent PADI utilized is less than 100 percent and the MOS for development toxicity and maternolethality are greater than 100, the section 18 for celery can be toxicologically supported.

Attachment

Avermectin toxicology review

Page _____ is not included in this copy.

Pages 5 through 8 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

X A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.